PROGRESS

OF

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MEDICINE.

UNDER THE CHARGE OF
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The Incidence of Alkaptonuria: A Study in Chemical Individuality. —GARROD (*The Lancet*, December 13, 1902, p. 1616), in a most interesting paper, gives the results of an investigation he has made concerning the blood relationship of the parents of individuals who are the subjects of alkaptonuria. It has now been amply shown that the properties of alkapton urine are due to the excretion of homogentisic acid first discovered by Wolkow and Baumann. The presence of this acid, causes the urine to darken with alkalies and on exposure to air, to stain fabrics a dark brown color and to reduce metallic salts. Its power to reduce copper solutions has led to an incorrect diagnosis of diabetes. Homogentisic acid is derived from tyrosin, but how and where this peculiar chemical change is brought about still remains unknown.

According to most observers alkaptonuria is regarded not as a manifestation of a disease, but rather as an alternative course of metabolism, which is harmless and usually congenital and life-long. This alternative metabolism is considered inferior to the usual plan, owing to a certain slight waste of potential energy. The amount of acid excreted daily varies within rather narrow limits in the recorded cases, the lowest being 3.2 grammes and the highest 5.9 grammes in the twenty-four hours.

The data regarding the incidence of alkaptonuria were gathered from the reports of the 40 cases that have appeared in the literature to date, and also from correspondence with the physicians who recorded the cases. The condition is nearly always congenital. Males are more frequently affected than females, the statistics showing 29 and 11 respectively. The abnormality is apt to occur in two or more brothers and sisters whose parents are normal and among whose forefathers there is no record of its having occurred, a form of incidence seen in other conditions. Thus, in 32 known examples, which were presumably congenital, 19 occurred in seven families. One family contained four alkaptonurics, three others three, and the remaining three two each.

Garrod's investigation appears to throw important light on the etiology of the condition. In 1901 he pointed out that of four British families in which were 11 congenitally alkaptonuric members no less than three were the offspring of marriages of first cousins who did not themselves exhibit this anomaly. He has carried the inquiry further, and has been able to secure information on this point in 19 of the 40 published cases. He found that 12 of these 19 cases, or more than 60 per cent., were the offspring of marriages of first cousins who did not themselves exhibit this anomaly. This is regarded as being very significant from the standpoint of etiology, and the suggestion is made that this high frequency may be explained by Mendel's law of heredity.

There is only one known instance in which the anomaly has been transmitted by an alkaptonuric father to his son. This case was observed by Osler, the individual being the son of one of the reported American cases. At the present time the condition of the urine of only five children of two alkaptonuric fathers is known. Only one of these children is himself alkaptonuric. That this proportion will be increased on further investigation does not appear probable to Garrod.

According to the writer, the view that alkaptonuria is a chemical "sport," or an alternative mode of metabolism is supported by the study of the incidence of albinism and of cystinuria. In the former males are also more frequently affected, and the offspring of first cousins are particularly liable to the anomaly. In the latter, again, the majority of the cases have been in males, but as yet the evidence of any influence of consanguinity of parents is not abundant. In both, the condition is more likely to occur in the children of parents who do not themselves exhibit the anomaly, thus clearly simulating alkaptonuria. Garrod thinks that it is quite probable that there are other examples of chemical "sports" that have not yet been discovered.

Diabetes Insipidus, with a Report of Five Cases.—FUTCHER (*The Johns Hopkins Hospital Reports*, vol. x. p. 197) reviews at some length the work that has been done on experimental polyuria in animals. In 1849 Bernard showed that there was a point in the floor of the fourth ventricle, just posterior to the Bernard diabetic centre, injury of which caused a simple polyuria. Investigation has shown that injury of other parts of the central nervous system will also give rise to a polyuria.

Clinically there are two classes of cases. First, the primary or idiopathic cases—those in which there is no evident organic basis for the disease. Second, the secondary or symptomatic cases—those attributable to definite organic changes, either of the nervous system or viscera. In some instances it is difficult to decide into which group certain border-line cases should be placed. Some observers classify those cases in which thirst is the first symptom as an independent disease under the name of primary polydipsia. As yet there does not seem to be sufficient evidence to warrant this.

Heredity is an important etiological factor. This is best illustrated by Weil's record of 23 cases among 91 members in four generations of one family. Tuberculosis, syphilis, gout, and general malnutrition were regarded